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BIOSIS / BIOSIS

AN - PREV200300265628

AU - Yamazaki V; Nguyen L; Schafer R J; Groves J T; Ulman N

AUAF- Proteomic Systems, Inc., Redwood Shores, CA, USA

CONF- American Society for Microbiology (ASM) Annual Meeting on Infectious Disease; San Diego, CA, USA; September 27-30, 2002

DT - Meeting, Meeting Poster, Meeting Abstract

LA - English

PCC - 00520, General biology - Symposia, transactions and proceedings

10508, Biophysics - Membrane phenomena

12512, Pathology - Therapy

22002, Pharmacology - General

25502, Development and Embryology - General and descriptive

38502, Chemotherapy - General, methods and metabolism

38504, Chemotherapy - Antibacterial agents

RN - 247145-86-4 (Alexa fluor 594)

AB - Background: With current antibiotic discovery activities and antibiotic use, antibiotic drugs have finite effective lives. As an example, even vanomycin, the glycopeptide "antibiotic of last resort," produces resistant strains of enterococci. The discovery of novel antibiotics is essential. We have investigated the MembraneChipTM to screen arrays of distinct microbial specific membrane targets simultaneously for novel antimicrobial drugs which operate via membrane disruption. Methods: The flat surface of a MembraneChipTM is designed to expose all features of the membrane target array to a single reagent at the same time. Lipid-bilayer corrals were filled with 99% egg phosphatidylcholine (PC, Avanti) with 1% NBD-phosphatidylglycerol (NBD, Avanti) by mole, except for one which contained 98% egg PC, 1% NBD and 1% ganglioside GM1 (Avanti). Then the entire chip was probed with fluorescent-labeled Cholera Toxin subunit B, Alexa Fluor 594 (Molecular Probes) at a concentration of 4µg/mL in phosphate buffered saline. The chip was visualized by fluorescence microscopy. Results: This MembraneChipTM experiment demonstrated the feasibility of using lipid-bilayer membrane arrays for antibiotic discovery, by utilizing the specific binding of the Cholera Toxin B subunits to the fluorescent ganglioside GM1, as an example of detecting a membrane binding/disrupting agent. Conclusions: This experiment demonstrates the MembraneChipTM as a platform for screening lipid targeting antimicrobial agents. MembraneChipsTM can be used to natively display many different microbial specific membrane targets to a large combinatorial peptide library for drug discovery.

AUC - USA

AW - ** Methods and Equipment **

MembraneChip, laboratory equipment; lipid-bilayer membrane array, applied and field techniques

- ** Alternate Indexing **

Bacterial Infections (MeSH)

IW - ** Major Concepts **

Equipment Apparatus Devices and Instruments; Infection; Membranes (Cell Biology) ; Methods and Techniques; Pharmacology

- ** Diseases **

bacterial infection: bacterial disease, drug therapy

- ** Chemicals and Biochemicals **

membrane-disrupting antibacterial agent: antibacterial-drug,
antiinfective-drug, phase I clinical trial, screening, development;
cholera toxin subunit B: toxin; Alexa fluor 594: toxin, Molecular
Probes, reagent

ORD - 2002-00-00

PD - 2002-00-00

PG - 194

PUB - Abstracts of the Interscience Conference on Antimicrobial Agents and
Chemotherapy

- 2002

TI - A novel technology for anti-microbial drug discovery.

VOL - 42

AUW - Yamazaki V; Nguyen L; Schafer R J; Groves J T; Ulman